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(54) **[Title of the Invention]**

Containers for radiopharmaceuticals and radiopharmaceutical preparations using said containers

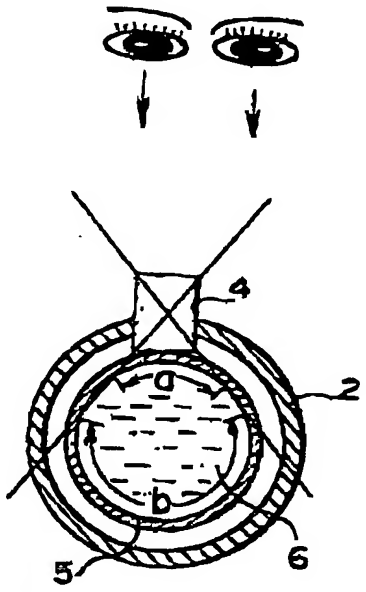
(57) **[Abstract]**

[Purpose]

To develop containers for pharmaceuticals which can prevent highly adsorbable radiopharmaceuticals from being adsorbed thereon and provide a clear description of their contents and the amounts thereof.

[Solution Means]

A container for radiopharmaceuticals in which the interior surface of a glass container is coated with silica and a container for radiopharmaceuticals in which reversed characters are written on the surface of a glass container.



[Claims]

[Claim 1]

A container for radiopharmaceuticals characterised in that the interior surface of a glass container is coated with silica.

[Claim 2]

A container for radiopharmaceuticals characterised in that reversed characters are written on the surface of a glass container.

[Claim 3]

A container for radiopharmaceuticals according to Claim 2 in which the shape of the glass container is cylindrical.

[Claim 4]

A container for radiopharmaceuticals characterised in that the interior of a glass container is coated with silica and reversed characters are written on the surface of the glass container.

[Claim 5]

A radiopharmaceutical preparation characterised in that a radiopharmaceutical container in which the interior surface of a glass container is coated with silica is filled with an adsorbable radioactive material.

[Claim 6]

A radiopharmaceutical preparation according to Claim 5 in which the adsorbable radioactive material is thallium chloride.

[Detailed Description of the Invention]

[0001]

[The Technical Field to which the Invention Pertains]

The present invention relates to containers for pharmaceuticals which are filled with radiopharmaceuticals and, more particularly, it relates to containers for pharmaceuticals which are filled with radiopharmaceuticals such as radioactive thallium chloride for transport and storage, and containers for pharmaceuticals on which descriptions are printed so that the nature of their contents can easily be confirmed.

[0002]

[The Prior Art]

Radioactive materials are used as tracers for diagnostic imaging in medical fields; in some cases a single element is used as the radioactive material and in other cases they are used by labelling compounds which show specific behaviour *in vivo*.

[0003]

Radioactive materials which are administered orally by means of capsules, etc. or intravenously by injection show *in vivo* distributions specific to the material, and the distributions are detected *ex vivo* using scintillation cameras or gamma cameras. The radioactivities so detected are shown in two-dimensional positional terms and as quantitative distributions; these distributions of radioactivity are grouped by colour using computer processing so giving images of radioactive movement *in vivo*. At present, the use of such techniques enables diagnostic imaging of myocardial disease areas and tumours.

[0004]

With regard to radioactive materials and tracers used for the above-mentioned diagnoses, radioactive thallium chloride as well as radioactive iodine, radioactive technetium, etc. can be cited. Since these radioactive materials are generally used as injections, they are supplied in glass vials or syringe type containers and there has been a desire for precise descriptions of the amounts on these containers so that the required amount of radioactive material can be correctly administered to the patient.

[0005]

However, there is the problem that radiopharmaceuticals such as, for example, radioactive thallium chloride (^{201}Tl) are sometimes adsorbed on the containers and in such cases even when a precise amount is measured, the required amount of the radioactive material cannot be administered to the patient. Although descriptions of the contents and the amounts thereof are usually printed directly on the surface of containers for pharmaceuticals, in the case of containers for radiopharmaceuticals they are often stored in lead-shielded containers equipped with a small lead glass window in order to reduce the exposure of the operators to radiation and it is hard to see the description of the contents and the amount thereof, which is a problem.

[0006]

Attempts have been made to solve the above-mentioned problem of the adsorption of radiopharmaceuticals on their containers by the use of plastic containers (Japanese Unexamined Patent 8-23829), the addition of a reducing agent (Japanese Unexamined Patent 6-256223), etc. Moreover, with regard to methods of describing the contents and the amount thereof, there have been attempts to achieve legibility by using brightly coloured paints, or wide or large characters.

[0007]

However, there are cases in which glass containers are easier to use than plastic containers and the use of reducing agents which are not directly related to the treatment or diagnosis is not desirable. If brightly

coloured paints are used, it becomes difficult to confirm the presence of the actual contents and if a means in which characters are enlarged, etc. is used there is the problem that the characters overflow the small lead glass window so making them illegible.

[0008]

[Problems to Be Solved by the Invention]

There has therefore been a desire for containers for pharmaceuticals which can prevent highly adsorbable radiopharmaceuticals from being adsorbed thereon and can give legible descriptions of the contents and the amounts thereof.

[0009]

[Means of Solving the Problems]

As a result of an intensive investigation by the present inventors in order to solve the above-mentioned problems, it has been found that glass containers whose interior surface is coated with silica can reduce the adsorption of radioactive thallium chloride (^{201}Tl) on the glass surface and they can be used as containers for radioactive thallium chloride injection liquids.

[0010]

Furthermore, it has been found that if a description of the contents, the amount thereof, etc. is written on the outside of the container for the pharmaceutical using reversed characters, the characters are enlarged to give good legibility due to the lens effect of the aqueous solution present inside the container, and furthermore by changing the viewing angle characters can be read over a wide area.

[0011]

That is to say, the present invention provides a container for radiopharmaceuticals characterised in that the interior surface of a glass container is coated with silica. The present invention further provides a container for radiopharmaceuticals characterised in that reversed characters are written on the surface of a glass container. Furthermore, the present invention provides a radiopharmaceutical preparation in which the above-mentioned container for radiopharmaceutical is filled with an adsorbable radioactive material.

[0012]

[Embodiments of the Present Invention]

The container for radiopharmaceuticals of the present invention in which the interior surface of a glass container is coated with silica (hereinafter, termed 'the first container') is prepared by placing a thermally volatile silicone (sic.) compound alone or a solution thereof in an alcohol, etc. inside an ordinary glass container for pharmaceuticals such as, for example, a vial, an ampoule or a syringe and subjecting it to a heat treatment. With regard to examples of the thermally volatile silicone (sic.) compound, silyl tetraisocyanate, silane gases, alkylsilanes, silane alkoxides, silicon halides, etc. can be cited. With regard to detailed methods of coating the interior surface of a glass container with silica, for example, a method disclosed in Japanese Unexamined Patent 2-175630 can be cited. In addition, since glass containers whose interior surfaces

have been coated with silica are commercially available under the product name of Silicoat (made by Fuji Glass Corp.), etc., these may be used.

[0013]

In the first container, the silica film coated on the interior surface of the glass container plays a role in preventing the pharmaceutical solution from coming into contact with water-soluble components such as alkalis included in the glass. That is to say, alkali components such as sodium ions (Na^+) and potassium ions (K^+) are present in the glass, and these components might be dissolved by the pharmaceutical solution. It is believed that in this solution state there is an equilibrium between the potassium ions and the glass; a constant amount of potassium ions is always present in solution, but potassium ions themselves change their state back and forth between the free state and the state in which they are bonded to the glass.

[0014]

When using an aqueous solution containing radioactive thallium chloride (^{201}Tl) as the radiopharmaceutical, since the thallium is present as a monovalent cation and not as a trivalent cation, it can be expected to show the same properties as those of potassium which is a monovalent cation. Since the thallium ions show the same properties as those of potassium ions, the potassium ions and thallium ions react with the glass competitively. As a result, a constant amount of thallium is always adsorbed on the glass. Therefore, even if a precise amount of the radiopharmaceutical is administered to a patient, it is short by an amount corresponding to the

amount of adsorbed thallium and the required amount of the radiopharmaceutical cannot be administered to the patient correctly.

[0015]

When the interior surface of the glass container is coated with silica, the dissolution of potassium from the glass can be suppressed, and thus the equilibrium reaction between thallium and potassium is not caused so preventing thallium from being adsorbed thereon.

[0016]

The container for radiopharmaceuticals of the present invention in which reversed characters are written on the surface of a glass container (hereinafter, termed 'the second container') is one in which reversed characters are written on the side opposite to the viewing side of a transparent container. The reversed characters in the present specification mean those which can be read as normal characters from the side opposite to the surface of the container on which the description has been made and can be read as reversed characters from the surface on which the description has been made.

[0017]

The second container can be obtained by directly printing reversed characters on the surface of a transparent container. It can also be obtained by printing reversed characters on a transparent label and sticking it to a transparent vial. The same effect can also be achieved by printing normal characters on a transparent label, coating an adhesive on the printed surface and sticking it to a glass vial. Furthermore, the same effect can be

achieved by printing normal characters on a non-transparent label, coating an adhesive on the printed surface and sticking it to a glass vial. By thus applying a description it can be read from the side opposite to the printed side.

[0018]

According to the second container, it is possible to enlarge small characters so making them legible by using the refraction of light in the container filled with a liquid and at the same time it is easy to confirm the presence of the contents. When viewing through the lead glass window of a protective container for radiopharmaceuticals in order to avoid direct viewing by the eyes and prevent exposure to radioactive materials, if normal characters are printed on the surface, only the area corresponding to the lead glass window is legible, but when printing is carried out with reversed characters, a wide area becomes legible by changing the viewing angle and furthermore the characters are enlarged due to the lens effect.

[0019]

The effect of the second container is explained in detail by reference to the drawings below. Fig. 1 is a front elevation of a protective container for radiopharmaceuticals and Fig. 2 is a cross-sectional view thereof through line A-A'. 1 is a protective container for radiopharmaceuticals, 2 is the main body of the protective container for radiopharmaceuticals, 3 is the lid of the protective container for radiopharmaceuticals, 4 is lead glass, 5 is the glass container and 6 is a pharmaceutical solution. 2 and 3 are made from an

exposure-preventing metal, generally lead, and it is impossible to see the inside **5** and read characters written thereon through **2** or **3**. On the other hand, since **4** is lead glass, it is possible to see the inside **5** and read characters written thereon through **4**.

[0020]

Fig. 3 is a sketch showing the range over which characters can be read in each case. When normal characters are written on **5**, only the characters on the area corresponding to **4** , that is to say, the area denoted by a, can be read. On the other hand, when reversed characters are written on **5**, although it is possible to read them as illegible reversed characters in the above-mentioned area **a**, characters on the opposite side (diagonal lines) are enlarged due to the lens effect if **5** is filled with a transparent pharmaceutical solution and they can be read as normal characters. By changing the viewing angle relative to **4**, characters over a wide area, that is, the opposite area denoted by **b**, can be read.

[0021]

[Effects of the Invention]

When the first container of the present invention is used as a container for radiopharmaceuticals, in particular a pharmaceutical container for radioactive thallium chloride, by measuring the required amount of radioactive material the precise amount can be administered.

[0022]

According to the second container of the present invention, even when viewing through lead glass, reversed

characters printed on the glass container are enlarged due to the lens effect caused by the container itself and its contents even though it is a small window; by changing the viewing angle a wide area can be read and thus the characters can be easily read.

[0023]

[Embodiments]

Below, the present invention is explained further in detail by reference to examples, but it is in no way limited thereby.

[0024] **Example 1**

Vials for radioactive thallium chloride: The vials of the present invention were obtained by coating the interior surface of 15 glass vials with silica by the method disclosed in an Example of Japanese Unexamined Patent 2-175630. For comparison, 15 glass vials without a silica coating were used (comparative vials). Each vial was filled with 1 ml of an injection solution of radioactive thallium chloride (^{201}Tl) (made by Daiichi Radioisotope Research Centre) and allowed to stand at room temperature for a fixed time so that the thallium could be adsorbed on the glass wall. After that, the solution was discarded, the container was washed with 1 ml of a physiological saline for injection and after discarding the washing liquid the remaining radioactivity of each vial was measured using a solid state detector (made by Seiko EG&G Corp.). The rate of adsorption of radioactive thallium was calculated from the radioactivity remaining relative to the radioactivity introduced. The results are given in Table 1.

[0025]

[Table 1]

Time standing (hr)	Present vial		Comparative vial	
	Radioactivity (cpm)	Adsorption (%)	Radioactivity (cpm)	Adsorption (%)
0.5	1	0.0	1618	6.8
1	5	0.0	1975	8.3
2	1	0.0	1997	8.4
6	2	0.0	2076	9.0
48	1	0.0	2218	11.8

[0026]

From the results above, it was found that adsorption of radioactive thallium chloride on the vial of the present invention coated with silica was greatly suppressed and it could be said to be almost none in comparison with the comparative vial.

[0027] **Example 2**

Vials for elution of radioactive technetium: Normal characters and reversed characters having a width of about 1 mm were written on vials for elution of radioactive technetium (made by Daiichi Radioisotope; diameter 25 mm; hereinafter termed 'collecting vials'). The vial on which normal characters were written was filled with 5 ml of physiological saline and loaded in a shielding container with lead glass (made by Daiichi Radioisotope Research Centre) and it was viewed through the lead glass (normal observation). The vial on which reversed characters were written was also filled with 5 ml of physiological saline and set on diagonal lines relative to the lead glass, and the contents and characters were viewed (diagonal line observation). The results are given in Table 2.

[0028]

[Table 2]

	Size of observed characters	Notes
Normal observation	1 mm	Characters were viewed with no effect from the liquid.
Diagonal line observation	About 1.5 mm	Enlarged characters were viewed due to the presence of the liquid.

[0029]

As is clear from the results above, enlarged characters could be viewed by using reversed characters and carrying out diagonal line observation through the lead glass window, and the presence of a liquid in the container could be confirmed at the same time.

[0030] **Example 3**

5 ml glass vial: A small diameter glass vial (diameter 15 mm: made by Fuji Glass Co., Ltd.) was used as a substitute for a radioactive pre-filled syringe, normal and reversed characters were written on the surface of the vial and the legibility of the characters was tested in the same manner as in Example 2. The results are given in Table 3.

[0031]

[Table 3]

	Size of observed characters	Notes
Normal observation	1 mm	Characters were viewed with no effect from the liquid.
Diagonal line observation	About 2 mm	Enlarged characters were viewed due to the presence of the liquid.

[Brief Explanation of Drawings]

[Fig. 1] Front elevation of a protective container for radiopharmaceuticals.

[Fig. 2] Cross-sectional view of Fig. 1 through line A-A'.

[Fig. 3] Sketch showing the range over which characters can be read.

[Explanation of Numerical Keys]

1 ··· Protective container for radiopharmaceuticals

2 ··· Main body of the protective container for radiopharmaceuticals

3 ··· Lid of the protective container for radiopharmaceuticals

4 ··· Lead glass

5 ··· Glass container

6 ··· Pharmaceutical solution

a ··· Range over which normal characters can be read.

b ··· Range over which reversed characters can be read.

Fig. 1

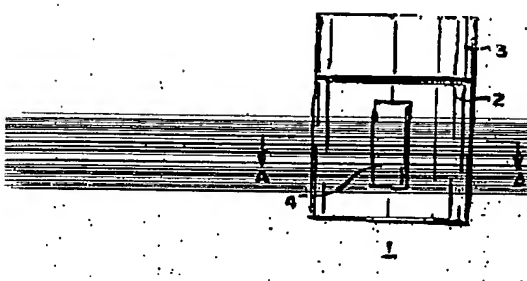


Fig. 2

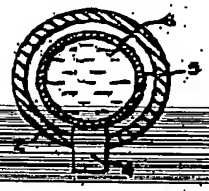


Fig. 3